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2300-0037.04
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PATRICIA C. NUNES
Typed or Printed Name of Person Mailing Paper or Fee

Patricia C. Nunes
Signature of Person Mailing Paper or Fee

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

COUSENS et al.

Serial No.: CON of 08/449,070 Group Art Unit: Unassigned

Filing Date: Herewith Examiner: Unassigned

Title: EXPRESSION USING FUSED GENES PROVIDING FOR PROTEIN PRODUCT

BLANKET PETITION FOR EXTENSION OF TIME AND AUTHORIZATION TO CHARGE OR CREDIT DEPOSIT ACCOUNT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

If a paper is untimely filed in this application or any file wrapper continuation application derived therefrom by applicant(s) or her/his/their representative, the Commissioner is hereby petitioned under 37 C.F.R. § 1.136(a) for the minimum extension of time required to make said paper timely. In the event a petition for extension of time is made under the provisions of this paragraph, the Commissioner is hereby requested to charge any fee required under 37 C.F.R. § 1.17(a)-(d) to Deposit Account No. 18-1648. This, however, is not authorization to pay the issue fee.

If a paper is concurrently or subsequently filed in this application or any file wrapper continuation application derived therefrom by applicant(s) or her/his/their representative and a fee under 37 C.F.R. §§ 1.16-1.17 is required to effect any amendment, petition or other action requested in said paper, the Commissioner is hereby requested to charge any deficiency in said fee, or credit any overpayment of said fee, to Deposit Account No. 18-1648. This, however, is not authorization to pay the issue fee.

Respectfully submitted,

Date: 8/16/01

By: _____
Roberta L. Robins
Registration No. 33,208

CHIRON CORPORATION
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"Express Mail" Mailing Label No. **EL 873 906 645 US**
Date of Deposit **August 16, 2001**

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PATRICIA K. HOLMES
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Patricia K Holmes
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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COUSENS et al.

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PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This Amendment is filed with a Rule 1.53(b) application. Entry of the following amendments is requested prior to examination.

I. AMENDMENTS

In the specification:

On page 1, please replace the paragraph beginning on line 5 with the following:

--This application is a continuation of U.S. Serial No. 08/449,070, filed 24 May 1995, which is a continuation of U.S. Serial No. 08/088,566, filed 6 July 1993 which is a continuation-in-part of U.S. Serial No. 07/680,046, filed 29 March 1991, which is a continuation of application Serial No. 07/169,833, filed 17 March 1988, which is a continuation-in-part of U.S. Serial No. 717,209, filed 28 March 1985, from which priority is claimed pursuant to 35 U.S.C. § 120, and which applications are incorporated herein by reference in their entireties.--

In the claims:

Please cancel claims 1-17, without prejudice or disclaimer.

Please add new claims 18 to 23 as follows:

18. (New) A method for producing a heterologous polypeptide comprising

(a) introducing a DNA sequence coding for a fusion polypeptide comprising the heterologous polypeptide and superoxide dismutase into a host cell;

(b) culturing the host cell under conditions such that the fusion polypeptide is expressed; and

(c) isolating the fusion polypeptide from the host cell.

19. (New) The method of claim 18, wherein the host cell is a prokaryotic cell.

20. (New) The method of claim 19, wherein the prokaryotic host cell is *E. coli*.

21. (New) The method of claim 19, wherein the prokaryotic host cell is *B. subtilis*.

22. (New) The method of claim 20, wherein the heterologous polypeptide is a mammalian polypeptide.

23. (New) The method of claim 21, wherein the heterologous polypeptide is a mammalian polypeptide.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendments. The attached pages are captioned "**Version with markings to show changes made.**"

II. REMARKS

New claims 18-23 have been added and find support throughout the specification as filed, for example on page 3, lines 24-30. Entry of the amendments is respectfully requested. These amendments obviate all previous rejections. Applicants note that these amendments are made solely to advance prosecution and are not in any intended as an acknowledgment that the Examiner's position in the parent case was correct.

The Examiner is requested to direct all further communication in this application to:

Lisa M. Alexander
Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097
Telephone: (510) 923-2585
Facsimile: (510) 655-3542.

Respectfully submitted,

Date: Aug 16, 2001

By: D Pasternak

Dahna S. Pasternak
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Attorney for Applicants

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Version with markings to show changes made to claims

1-17. Canceled.

18. (New) A method for producing a heterologous polypeptide comprising
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19. (New) The method of claim 18, wherein the host cell is a prokaryotic cell.

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VERSION SHOWING CHANGES MADE TO SPECIFICATION

CON OF USSN 08/449,070

IMPROVED EXPRESSION USING FUSED GENES PROVIDING FOR PROTEIN PRODUCT

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. Serial No. 08/449,070, filed 24 May 1995, which is a continuation of U.S. Serial No. 08/088,566, filed 6 July 1993 which is a continuation-in-part of U.S. Serial No. 07/680,046, filed 29 March 1991, which is a continuation of application Serial No. 07/169,833, filed 17 March 1988, which is a continuation-in-part of U.S. Serial No. 717,209, filed 28 March 1985, from which priority is claimed pursuant to 35 U.S.C. § 120, and which applications are incorporated herein by reference in their entireties.

BACKGROUND OF THE INVENTION

Field of the Invention

There are an increasingly large number of genes available for expression, where the expression product may find commercial use. In many instances, the initial expression has been observed in *E. coli*. Expression in *E. coli* has many disadvantages, one in particular being the presence of an enterotoxin which may contaminate the product and make it unfit [to] for administration to mammals. Furthermore, there has not previously been an extensive technology concerned with the production of products in *E. coli*, as compared to such other microorganisms as *Bacillus subtilis, Streptomyces*, or yeast, such as *Saccharomyces*.

In many situations, for reasons which have not been resolved, heterologous products, despite active promoters and high copy number plasmids, are produced in only minor amount, if at all, in a microorganism host. Since the economics of the processes are dependent upon a

SUBSTITUTE COPY OF PAGE 1 OF SPECIFICATION

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